Original Article

Evaluation of therapeutic outcomes in emphysematous pyelonephritis: a single-center experience at Siriraj Hospital

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Abstract

Objective: Emphysematous pyelonephritis (EPN) is an acute, severe, necrotizing parenchymal and perirenal infection associated with high morbidity and mortality. The radiographic classifications, which determine the treatment strategies, however, remain controversial. Our study aimed to evaluate and compare the clinical parameters related to nephrectomy and the treatment outcomes in current practices.

Materials and Methods: We retrospectively reviewed the data from 21 EPN patients who had been diagnosed using computed tomography (CT) scans, who were admitted to Siriraj Hospital from January 2009 to December 2019. The clinical manifestations, imaging results, laboratory findings, treatment methods, and overall outcomes of each patient were reviewed and analyzed. Huang–Tseng's and Wan's classifications were used to classify the images obtained from the CT scans.

Results: Among the 21 patients with EPN, all had at least one comorbidity associated with a compromised immune response. Common manifestations included fever (74%) and initial laboratory findings showed hyperglycemia (66%), acute kidney injury (72%), and metabolic acidosis (76%). Inotropes were used in 13 patients for hemodynamic support. Eleven patients were treated with a non-nephrectomy approach, while 10 patients underwent nephrectomy. No statistical difference in treatment outcomes was observed between groups in both classification systems. Overall survival was 100% with a minimum one-year follow-up.

Conclusion: Our study demonstrated that the current treatment approach has resulted in a zero mortality rate of EPN most probably due to advancements in antibiotics, surgical techniques, and postoperative intensive care over the years. However, refining treatment strategies, considering radiographic criteria, clinical parameters, and initial treatment response, is essential in future studies to further decrease disease morbidity.

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Introduction

Emphysematous pyelonephritis (EPN) is an acute and severe necrotizing parenchymal and perirenal infection caused by gas-forming uropathogens.[1] While uncommon, it is a serious condition with high morbidity and mortality rates of up to 40%-50%.[2,3] However, over the last two decades, the mortality rate has decreased to 20% due to the introduction of a new generation of antibiotics and the use of better surgical techniques.[4]

In the past, open drainage and the use of antibiotics regardless of nephrectomy was the standard treatment.[5,6] More recently, there has been a shift towards disease classification using computed tomography (CT) scans to determine prognosis and guide appropriate treatment options. The results to date have been promising, especially when considering the role of nephrectomy regarding imaging classifications.[7,8] However, ideal management processes remain controversial and should be personalized for each patient.

In the era of modern perioperative-, intensive-, and critical-care specialists, the outcomes of EPN treatment have improved. This study aims to investigate EPN treatment outcomes at Siriraj Hospital and to compare the factors based on image classifications and the association with nephrectomy.

Materials and Methods

Following Institutional Review Board approval (Protocol Number 353/2563 (IRB4)), we conducted a retrospective review of EPN patients admitted to Siriraj Hospital between January 2009 and December 2019. A total of 21 patients were diagnosed with EPN using a CT scan. The clinical manifestations, radiographic findings, laboratory results, treatment modalities, and outcomes were reviewed and analyzed.

In our study, two image classifications were utilized to categorize patients, specifically those of Huang and Tseng[8] and Wan et al.[7] According to Wan et al., Type 1 classification is defined as EPN with parenchymal destruction and an absence of fluid content, while Type 2 refers to EPN with the presence of renal or perinephric fluid associated with a loculated gas pattern. Huang and Tseng's system categorizes EPN into four types: type 1 - gas in the collecting system only; type 2 - gas in the parenchyma without extending into the extrarenal space; type 3a - extension of gas or abscess into the perinephric space; type 3b - extension of gas or abscess into the pararenal space; and Type 4 - bilateral EPN or EPN in a solitary kidney.

Previous studies indicate that type 1 and type 2 EPN under the Huang-Tseng classification exhibit a lower mortality rate (0-10%) compared to types 3a, 3b, and 4 (20%-50%).[7,8] Therefore, in the present study, we categorized patients into two groups based on the Huang-Tseng classification: group 1 comprising type 1 and type 2, and group 2 comprising Type 3 and Type 4 EPN cases.

Additionally, we examined factors associated with nephrectomy in EPN patients. There are six laboratory factors that may result in adverse clinical outcomes: hyperglycemia, defined as initial blood glucose > 11.10 mmol/l; anemia, defined as hematocrit (HCT) < 30%; leukocytosis, defined as white blood cell (WBC) count >12x09/l; thrombocytopenia < 100x109/l; metabolic acidosis, defined as serum bicarbonate < 20 mmol/l and blood pH < 7.2; and acute kidney injury, defined as a decreased glomerular filtration rate (GFR) > 30% of baseline or serum creatinine > 0.13 mmol/l.[9] The outcomes assessed were the treatment modality, i.e., nephrectomy or non-nephrectomy (medication, ureteral stent, or percutaneous drainage), long-term renal replacement therapy (RRT), and mortality rate.

Statistical analysis

Quantitative variables are presented as mean (minimum, maximum), while qualitative variables were reported as frequency and percentage. Chi-square and Fisher's exact tests were used to compare categorical variables, and the Mann-Whitney U test was employed to compare continuous variables between radiographic classifications type 1 and type 2. Statistical significance was defined as a p-value of less than 0.05. PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, USA) was used for the statistical analysis.

Results

During a 10-year-period, a total of 21 patients were diagnosed with EPN (20 females and 1 male) at our institute. The mean age was 55.2 years (range 30-72). Seventeen patients (80%) had diabetes mellitus, with six (35%) being newly diagnosed. Other comorbidities included hyper-

tension (33%), chronic kidney disease (28%), the use of immunosuppressive drugs (23%), previous urological stones (21%), history of urological surgery (14.3%), and cirrhosis (9.5%). All patients had at least one comorbidity associated with a compromised immunologic response, (Table 1).

As shown in Table 2, the most common clinical manifestation was fever (74%), followed by tachycardia (71%), flank pain (66%), alteration of consciousness (23%), dysuria (19%), and hematuria (14%). Seven patients (33%) were diagnosed with septic shock and another seven (33%) with diabetic ketoacidosis upon initial presentation. Predominant pathogens included *Escherichia coli* (80%), Klebsiella pneumoniae (14%), and Proteus mirabilis (6%), constituting extended-spectrum beta-lactamases (ESBL) strain microorganisms, accounting for 38%. Initial laboratory abnormalities included hyperglycemia (66%), anemia (61%), leukocytosis (57%), thrombocytopenia (42%), acute kidney injury (71%), and metabolic acidosis (76%).

All patients received initial intravenous antimicrobial treatment, including meropenam (81%) and piperacillin/tazobactam (19%). Inotropic drugs were used in 13 patients (62%) to maintain hemodynamics. Eleven patients (68%) were treated with non-nephrectomy approaches while 10 (34%) underwent nephrectomy. The survival rate was 100% at one-year follow-up, no deaths being observed.

Table 1. Characteristics of 21 patients diagnosed with EPN

Characteristics	Patients with EPN (N=21)
Age (mean, range, years)	55.2 (30-72)
Sex (n, %)	
Male	1 (5)
Female	20 (95)
Total	21 (100)
Comorbidities (n, %)	
Diabetes mellitus	17 (80)
Hypertension	7 (33)
Chronic kidney disease	6 (28)
Immunosuppressive drug usage	5 (23)
Previous urological stones	4 (21)
Previous urological surgery	3 (14.3)
Cirrhosis	2 (9.5)

EPN = emphysematous pyelonephritis

Table 2. Characteristics of 21 patients diagnosed with EPN

Variables	Number (%) of patients (N=21)
Clinical features	
Fever	15 (71)
Flank pain	14 (66)
Dysuria	4 (19)
Tachycardia	15 (71)
Hematuria (microscopic, gross)	3 (14)
Alteration of consciousness	5 (23)
Septic shock	7 (33)
Diabetic ketoacidosis	7 (33)
Laboratory results	
Hyperglycemia (blood glucose > 11.10 mmol/l)	14 (66)
Anemia (Hct < 30%)	13 (61)
Leukocytosis (WBC >12x10^9/l)	12 (57)
Thrombocytopenia (platelet < 100x10^9 /l)	9 (42)
Metabolic acidosis (serum bicarbonate < 20 mmol/l)	16 (76)
Acute kidney injury	15 (71)
Treatment strategies	
Inotropic medication	13 (62)
Approaches	
Non-nephrectomy	11 (68)
Nephrectomy	10 (34)
Total	21 (100)

EPN = emphysematous pyelonephritis, WBC = white blood cells, Hct = hematocrit

Table 3. Baseline characteristics and treatment outcomes of patients with EPN classified by Wan's classification

Factors	Type 1 (n=5)	Type 2 (n=16)	P-value
Age (years) ≥ 65	2	2	0.22
Sex			1.00
Male	0	1	
Female	5	15	
Diabetes mellitus	2	11	0.32
Chronic kidney disease	2	4	0.59
Nephrectomy	3	7	0.64
Long-term RRT	2	1	0.13

EPN = emphysematous pyelonephritis, RRT = renal replacement therapy

The baseline characteristics and treatment outcomes, including nephrectomy and long-term RRT, are shown in Table 3 (Wan classification) and Table 4 (Huang-Tseng classification). No baseline differences were observed between the groups, and there was no statistical difference in treatment outcomes for both classifications. Clinical factors associated with nephrectomy were also analyzed, as shown in Table 5. No significant differences were found between the nephrectomy and non-nephrectomy groups, including in the alteration of consciousness, acute kidney injury, thrombocytopenia, and shock.

Table 4. Baseline characteristics and treatment outcomes of patients with EPN classified by Huang–Tseng's classification

Factors	Group 1 (n=9)	Group 2 (n=12)	P-value
Age (years) ≥ 65	3	1	0.27
Sex			1.00
Male	0	1	
Female	9	11	
Diabetes mellitus	6	7	1.00
Chronic kidney disease	3	3	1.00
Nephrectomy	4	6	1.00
Long-term RRT	2	1	0.53

EPN = emphysematous pyelonephritis, RRT = renal replacement therapy

Discussion

While EPN is uncommon, it remains a life-threatening condition. Over the past two decades, various studies have evaluated the prognostic factors associated with morbidity and mortality.[10-13] In 1996, Wan et al. introduced a classification system for EPN, categorizing it into two types based on radiographic criteria: type 1 which exhibited a higher mortality rate (69%) in comparison to type 2 (18%).[7] Subsequently, in 2000, Huang and Tseng classified EPN into four classes, classes 3 and 4 resulting in increased failure rates for conservative treatment (with up

Table 5. Factors associated with the nephrectomy and non-nephrectomy groups in patients with EPN

Factors	Nephrectomy (n=10)	Non-nephrectomy (n=11)	P-value
Age (years) ≥ 65	1	3	0.58
Diabetes mellitus	5	8	0.38
Chronic kidney disease	5	1	0.06
Alteration of consciousness	4	1	0.14
Diabetic ketoacidosis	5	2	0.18
Septic shock	3	5	0.65
Leukocytosis	4	8	0.19
Thrombocytopenia	5	4	0.67
Serum glucose > 11.10 mmol/l	8	6	0.36
Acute kidney injury	6	9	0.36
Metabolic acidosis			
Serum bicarbonate < 20 mmol/l	9	7	0.31
Arterial blood gas pH < 7.2	2	5	0.36

EPN = emphysematous pyelonephritis

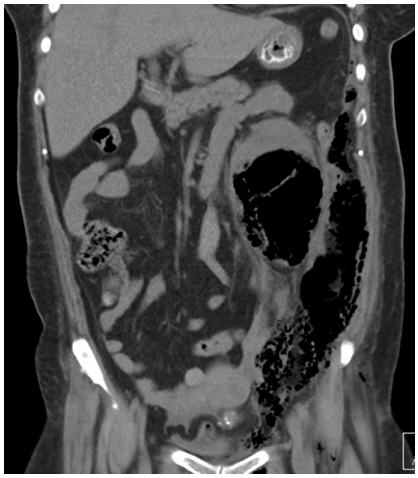
to 70%-75% of patients requiring nephrectomy) and mortality rates of 20%-50%.[8] A more recent study conducted in Taiwan by Tsu et al. in 2012 reported a reduction in the nephrectomy rate to 50% and mortality rate to 33% for EPN patients categorized by both Wan and Huang-Tseng criteria.[6] Similar results were also reported in a study by Olvera-Posada et al. in Mexico, where nephrectomy and mortality rates were reduced to 16% and 11%, respectively.[14]

The lack of established guidelines for treating EPN adds complexity to the clinical management of this condition. Historically, aggressive surgical interventions demonstrated superiority over medical treatments alone.[8] Nevertheless, morbidity and mortality were greater in early nephrectomy patients compared to those undergoing initial conservative strategies with percutaneous drainage (PCD) and antibioticstherapy.[8,14] Controversy persists over the efficacy of PCD in EPN patients.

Akpek et al. reported that 57% of patients in whom PCD was attempted experienced treatment failure, with a mortality rate of 26%.[15] In Huang and Tseng's study, 92% of patients classified as Classes 3 and 4 were reported to have PCD treatment failure, with a mortality rate of 15%. The clinical risk factors associated with poor outcome were thrombocytopenia, acute renal failure, altered mental status, and shock.[8] Additional studies by Falagas et al. and Kapoor et al. highlighted factors associated with increased mortality, namely an altered mental status, thrombocytopenia, acute renal failure, and severe hyperglycemia.[16,17] It is essential to take these factors, including imaging classification and several clinical features, into consideration when assessing treatment modalities.

Our approach involved initial resuscitation for fluid and electrolyte imbalance, hyperglycemic screening, and intravenous antibiotics in cases where urosepsis or septic shock was diagnosed. Subsequently, we monitored patients to assess their initial response to treatment. While imaging characteristics, disease extension, and clinical parameters such as mental status, severe metabolic acidosis, septic shock, or disseminated intravascular coagulation (DIC), and decreased renal function are crucial for determining the stage and severity of the disease, it is emphasized that these should not be routinely used as indicators for intervention or nephrectomy. Additional significant factors, including bacterial virulence, host immunity, hyperglycemic control, and the adequacy of blood supply for antibiotic delivery to the renal parenchyma, play pivotal roles in determining the response and necessity for surgical intervention following initial treatment.

Our study revealed no statistically significant factors associated with radiographic classifications, clinical parameters, or treatment modalities (Tables 3, 4). Intriguingly, some patients with extensive radiographic findings and challenging clinical parameters were successfully managed with a non-nephrectomy strategy. As shown in Figure 1, a patient with metabolic acidosis and extension of EPN to the anterior abdominal wall and pelvic cavity was effectively managed with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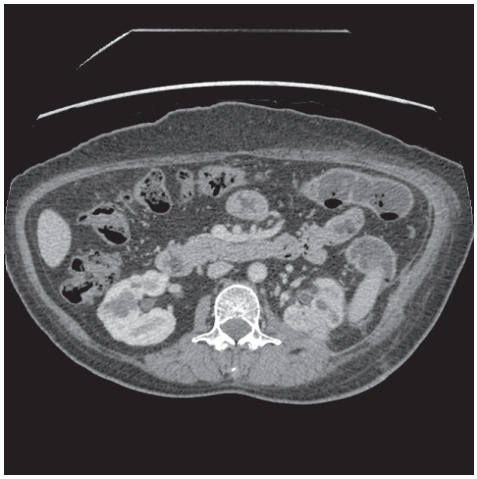
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Figure 1. (A) A 54-year-old female with left extensive emphysematous pyelonephritis extended to anterior abdominal wall and pelvic cavity. Blood gas pH was 7.24. She underwent left open drainage and was discharged with normal kidney function. (B) Follow-up imaging.

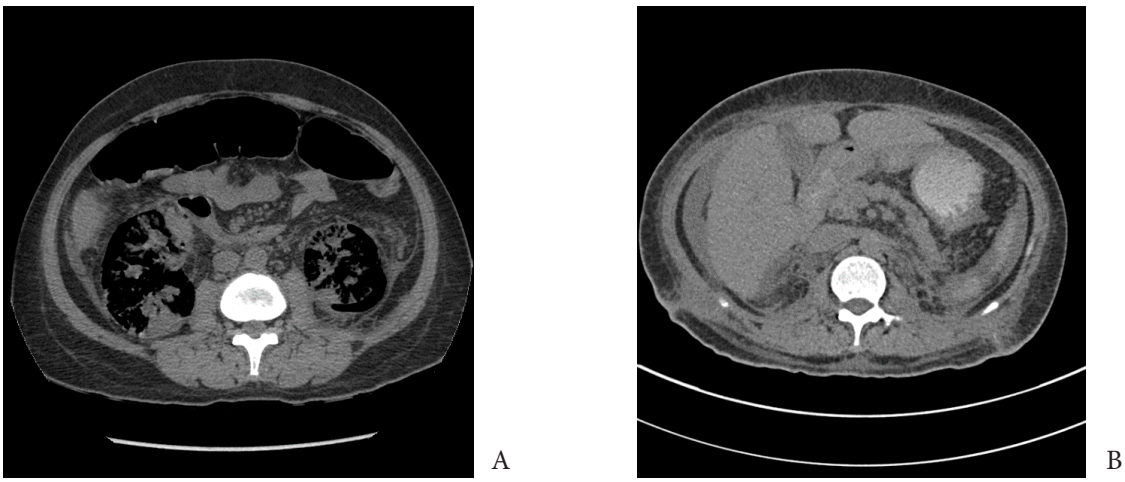

Figure 2. (A) A 51-year-old female with bilateral emphysematous pyelonephritis, blood gas showed severe metabolic acidosis (pH 7.15). She underwent bilateral nephrectomy and was discharged with long term dialysis. (B) Postoperative follow-up imaging.

intravenous antibiotics and open drainage, eliminating the necessity for nephrectomy. Conversely, some patients with less extensive radiographic findings and favorable clinical parameters eventually required nephrectomy due to worsening clinical conditions (Table 5). Similar to findings from previous studies[18-20], the initial treatment response played a crucial role in determining the treatment strategy at our institution. However, this was a retrospective study and the definition of treatment response for EPN, which is not well established, depended on individual experience.

In the present study, the nephrectomy rate was 50%, and no fatalities were observed. Perioperative care, the intervention of intensive care specialists, and the postoperative application of continuous RRT significantly contributed to positive treatment outcomes, as mentioned by Sokhal et al.[20] For instance, as depicted in Figure 2, a patient with bilateral EPN and Wan type 1 classification underwent bilateral nephrectomy due to clinical deterioration. The subsequent continuous RRT was successfully implemented, enabling the patient to survive with long-term hemodialysis. The reduction in morbidity and mortality rates of EPN over time has resulted not only from the improvement in the medication and surgical intervention approaches, but also from refined clinical judgment, improved perioperative care, and the effective application of modern technology.

The limitation of our study was its small sample size and lack of transferability as it was carried out in a single institution and as it is a relatively uncommon disease. A further multicenter study should be developed to validate the efficacy of the classifications. Our assessment of long-term outcomes was constrained by the limited follow-up period.

Conclusions

While emphysematous pyelonephritis is a life-threatening condition, the mortality rate has significantly decreased over time. It was reassuring to record a zero-mortality rate with the current treatment practices, potentially due to the current improvement in specific antibiotics, surgical techniques, and postoperative intensive care. Future studies should focus on refining treatment strategies based on radiographic criteria, clinical parameters, and the response to initial treatment to further enhance patient outcomes and reduce the morbidity associated with this disease.

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Conflicts of Interest

The authors declare no conflicts of interest.

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